ENVIRONMENTAL TOBACCO SMOKE

EXPOSURE STUDIES

A REVIEW OF THE LITERATURE

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ETS: A CHARACTERIZATION

- Environmental tobacco smoke (ETS) is an aged and dilute mixture of sidestream smoke (SS), or the smoke from the burning end of the cigarette, and exhaled mainstream smoke (MS), the smoke to which the smoker is exposed.

- ETS differs chemically and physically from both MS and SS. ETS is a dynamic, ever-changing mixture which, as it ages and dissipates, undergoes chemical reactions and physical change. There is no single definable, reproducibly characterizable entity known as ETS.

- Dissipative forces such as air currents and attraction to surfaces influence SS and exhaled MS. Studies indicate that constituents in ETS are hundreds to thousands of times more dilute than either SS or MS. Often, concentrations of ETS constituents fall below detection limits of current scientific measurement devices.

- As ETS ages, a number of physico-chemical changes take place. Matter evaporates from SS particles as they age to ETS. During the aging process, ETS particles coagulate and increase in size. Chemical compounds partition between the gas and

particle phase of the smoke. (For example, nicotine is found in the particle phase of MS; in fresh SS, most of the nicotine is in the gas phase.) Decay patterns for constituents of ETS vary over time and are dependent upon physical conditions in the environment.

- ETS is not equivalent to either MS or SS. Many studies and reviews employ sidestream/mainstream smoke comparisons, ostensibly to demonstrate the kind and quantity of constituents involved in exposure to ETS. But such comparisons are deceptive and misleading. As two tobacco smoke chemists reported in 1990:[1]

> Although ETS originates from sidestream and exhaled mainstream smoke, the great dilution and other changes which these smoke streams undergo as they form ETS make their properties significantly different from those of ETS. Thus, the sidestream/mainstream ratios quoted in Table 1 can be misleading if used out of context. The important question is not the ratio of sidestream/mainstream but rather what is the concentration of the constituent in the indoor environment and how does it compare to levels from sources other than ETS. Studies based solely on observations of fresh sidestream, or highly and unrealistically concentrated ETS, should take into account the possible differences between these smokes and ETS found in real-life situations.

• Even the 1986 Report of the Surgeon General on ETS and the 1986 NRC/NAS Report on ETS conceded:

> Comparison of the relative concentrations of various components of SS and MS smoke provides limited insights concerning the toxicological potential of ETS in comparison with active smoking. As described above, SS characteristics, as measured in a chamber, do not represent those of ETS, as inhaled by the non-smoker under nonexperimental conditions.[2]

Similarly, the NAS Report concluded:

> Because the physicochemical nature of ETS, MS, and SS differ, the extrapolation of health effects from studies of MS or of active smokers to nonsmokers exposed to ETS may not be appropriate . . . .[3]

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EXPOSURE TO ETS

- Published studies indicate that nonsmoker exposure to ETS under normal, everyday conditions is minimal. For example, researchers report that there is little difference in ambient levels of carbon monoxide in smoking and nonsmoking areas of workplaces and public places and in homes with and without smokers.[1-6] Other studies indicate that ETS contributes less than half of the total particles in the air of a typical public place.*[7-14] Nicotine is often used as a marker for ETS

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* A paper published in a 1980 issue of Science magazine, in which the authors reported the results of their efforts to measure particles or particulates in the air of smoking and nonsmoking areas, is often cited to support the claim that ETS is a major indoor pollutant. The authors, Repace and Lowrey, contend that the levels of particles they observed in the smoking areas were much higher than in the nonsmoking areas. However, their study results are inconsistent with many others. For example, the average particle count attributed to ETS in their study was from three to twenty times higher than the average levels reported in other studies of office buildings, restaurants and residences.

There are a number of explanations for the authors' apparent overestimation of ETS exposure. First, they selectively sampled environments such as meeting and game rooms, bars and sandwich shops which did not represent normal occupancy conditions and where particulate levels would likely be high regardless of the presence or absence of tobacco smoke. Second, through inappropriate testing methods, they incorrectly assumed all particles in the air arose from ETS. However, as several researchers have noted, ETS typically contributes about one-third of the overall particle levels in indoor spaces. Moreover, particles also are generated by people and their everyday routine activities such as movement and cooking. (Repace, J. and A. Lowrey, "Indoor Air Pollution, Tobacco Smoke and Public Health," Science 208: 464-472, 1980.)

exposures because it is unique to tobacco smoke. Typical measurements of nicotine range from an exposure equivalent of 1/100 to 1/1000 of one filter cigarette per hour.[15-22] This means that a nonsmoker would have to spend from 100 to 1000 hours in an office, restaurant or public place in order to be exposed to the nicotine equivalent of a single cigarette.

- Studies which have examined ETS constituent levels of nitrosamines, nitrogen oxides and volatile organic compounds (such as benzene**) report minimal contributions to overall ambient air levels in homes, the workplace and public places.[23-36]

** Benzene exposure from ETS is negligible, despite reports to the contrary.[37-38] "Automotive fuel is, by far, the largest, most pervasive source of benzene exposure. In 1989, the U.S. Department of Health and Human Services estimated that 1 billion pounds of benzene were released into the atmosphere from the refueling and operation of approximately 130 million motor vehicles in 1976 [NIEHS, 1989]. This translates into 7.8 pounds of benzene per vehicle per year. In contrast, a pack-per-day smoker would generate approximately 0.008 pounds of benzene per year, assuming that, at most, 0.5 mg of benzene is generated from one cigarette (MS plus SS) [Hoffmann, 1990]. Based on these estimates, an average person is potentially exposed to 1,000 times more ambient benzene from one automobile than from a smoker in a given year." [From: Response of RJR, The U.S. EPA: "ETS: A Guide to Workplace Smoking Policies," October 1, 1990.]

Questionnaire Reliability:

- All of the epidemiologic studies on the purported association between ETS exposure and disease in nonsmokers rely solely upon questionnaires about exposure, rather than upon actual exposure data.[39-41] Recent studies indicate that questionnaires are an unreliable and inaccurate measure of exposure. Questionnaire responses about exposure vary widely when compared with actual measurements of ETS constituents in the ambient air.[41]

ETS and Radon:

- A theory that suggests that concentrations of radon decay products increase in the presence of tobacco smoke, thus implying an increased risk of lung cancer for the nonsmoker, has been reported in the literature.[42-44] The theory suggests that radon decay products attach to particles (including ETS) in the air, remain suspended, and are subsequently taken up in the lungs of nonsmokers.

- However, actual data indicate that this is not the case.[45-48] It is the unattached, gaseous fraction of radon which determines the dose of radiation to the respiratory tract. According to these data, as dust or particulate levels

increase, the unattached fraction of radon daughters will decrease, thereby lowering the potential dose of radiation to the lungs.

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DETERMINATION OF DOSE: COTININE

- It has been reported that cotinine, a substance converted from nicotine by the body, can be used as a biological marker to measure nonsmoker exposure to ETS.[1-2] While some reports suggest that cotinine is a reliable marker for total exposure to tobacco smoke, many others do not.[3-12] Researchers have reported that individuals metabolize nicotine in different ways at different times and that elimination rates for cotinine vary among individuals. In addition, recent research indicates that diet may contribute to levels of nicotine and cotinine found in the body, thereby interfering with ambient air exposure levels.[13] Scientists have also noted that different methods of analysis may influence final recorded levels of cotinine.[14] And finally, because cotinine is a metabolite of a gas-phase constituent of ETS, nicotine, cotinine levels do not represent exposures to other constituents of ETS.

- In conclusion, cotinine is not a reliable quantitative measure of ETS exposure. This is because body fluid levels of cotinine cannot be attributed solely to nicotine in ETS, and because body fluid levels of cotinine do not correlate well with actual ambient air exposures to ETS or with ETS constituents other than nicotine. At best, cotinine may be used as a qualitative marker of ambient nicotine exposures.

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DETERMINATION OF DOSE: LUNG RETENTION

- Cotinine is a biologically inactive substance which has not been correlated with ETS constituents retained in the lung. Several researchers have estimated levels of ETS particulate uptake by nonsmokers to approximate 0.02% (two-hundredth of one percent) that of the particulate exposure of an active smoker.[1-4]

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DETERMINATION OF DOSE: MUTAGENS

- Some reports have suggested that the potential toxicity of ETS can be assessed by measuring mutagens in the body fluids of nonsmokers exposed to ETS.[1-3] Mutagens are substances capable of altering the genetic structure of cells. It is suggested that the presence of mutagens in body fluids (e.g. urine) may be an indication that an individual has been exposed to substances capable of inducing cancer.

- Impetus for the theory arises, in part, from studies which report that various constituents of ETS collected through airborne samples are capable of inducing mutations in bacteria.[4-6]

- However, the significance of such reported findings has not been established. Virtually all air samples, whether in the presence or absence of smoking, are mutagenic. Indeed, no substance, including food and natural materials, has been unequivocally shown to be free of carcinogenic and/or mutagenic properties. In addition, it has been reported that sidestream smoke exhibits diminished mutagenic activity as it ages and becomes diluted (i.e., as it becomes ETS).[7]

- With few exceptions, studies which have compared mutagens in the body fluids of nonsmokers exposed to realistic levels of ETS and nonsmokers not exposed to ETS report no significant difference in mutagenic activity.[8-11]

- The few studies reporting significant increases in urinary mutagenicity among individuals exposed to ETS[1-3] did not employ realistic levels of exposure to ETS, and they did not control adequately for the presence of mutagens in the diet of the study subjects.

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DOSE: OTHER BIOLOGICAL MARKERS

- It has been suggested that sidestream smoke (and by inference, ETS) contains polycyclic aromatic hydrocarbons (PAH), substances which have been designated as carcinogens by various governmental agencies. However, in a series of papers, German researchers report no significant differences in urinary PAH by-products among nonsmokers exposed to ETS and those not exposed.[1-3] Diet was reported to have a profound influence on PAH by-product formation in all study subjects.

- Japanese scientists have reported that individuals exposed to ETS have increased urinary levels of hydroxyproline (HOP), a substance believed to act as a marker for the breakdown of lung tissue.[4] However, German researchers have reported no increase in HOP excretion among either smokers or nonsmokers exposed to ETS.[5]

- It has recently been suggested that DNA adducts can be utilized as biomarkers to assess exposure (dose) to ETS.[6] (An adduct is a product derived from reactions between chemicals and biological material (such as DNA)). Research, however, does not conclusively support this theory; nonsmokers exposed to ETS do not appear to exhibit increased DNA adduct production.[7] Other studies report no increased chromosomal changes in body

fluids of nonsmokers exposed to ETS.[8-9]

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BIOLOGICAL PLAUSIBILITY

- The argument for the biological plausibility of the role of ETS in disease causation depends upon the simplistic claim that since mainstream (MS) and sidestream (SS) smoke contain carcinogenic substances, so must ETS. However, this analogy is not proved.

- ETS has never been shown to be carcinogenic in any animal species. Only two animal inhalation experiments investigating ETS and lung cancer have been published. Both studies report no meaningful histopathological differences between animals exposed to ETS and those which were not exposed. In a study conducted by the American Health Foundation,[1-3] the investigators exposed one group of hamsters to mainstream smoke and another group to ETS. Animals exposed to mainstream smoke and ETS lived longer than the sham treated controls. The investigators reported that overall there was no marked increase in tumor incidence in animals exposed to either mainstream smoke or ETS after 18 months of exposure. The second study was a 90-day ETS inhalation study of rats and hamsters.[4] Animals were exposed to ETS concentrations 100 times those concentrations encountered by nonsmokers. These researchers reported no histopathological differences between exposed and control animals. Electron microscopy revealed

pulmonary changes which could be expected to occur under similar exposure conditions with other substances.

- In addition, recent reviews of the literature on suspected pulmonary carcinogens have indicated that none of the individual constituents in sidestream smoke classified as potentially carcinogenic has been found to induce pulmonary cancer via inhalation in experimental animals.[5-6]

- ETS has not be shown to be mutagenic in any animal or cell culture system when tested at realistic levels of exposure (See Section III).

- These points undermine the credibility of the argument for the biological plausibility of ETS in disease causation.

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